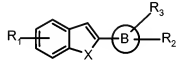
Amendments to Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended): A method of treating ~~or inhibiting~~ a disorder associated with the activation of large conductance calcium activated potassium channels, wherein the disorder is selected from the group consisting of: urinary incontinence, overactive bladder, and pollakiuria, ~~urge incontinence, diseases associated with detrusor instability, irritable bladder, cystitis, urethritis, and kidney stone ailments,~~ which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I):



(I)

wherein:

R_1 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, trifluoromethyl, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, $(C_{1-}$

$_6$)alkylsulfoxyl, -N(R')$_2$, -CH$_2$N(R')$_2$, nitro, cyano, -CO$_2$R', -CON(R')$_2$, -COR', and -NR'C(O)R';

each R' is independently H or unsubstituted (C_{1-6})alkyl;

X is NR_a

B is phenyl;

R_2 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, -N(R')$_2$, -CH$_2$N(R')$_2$, nitro, cyano, -CO$_2$R', -CON(R')$_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, -N(R')$_2$, -CH$_2$N(R')$_2$, nitro, cyano, -CO$_2$R', -CON(R')$_2$, -COR', and -NR'C(O)R';

R_3 is COOH, $CONR_aR_b$, SO_3H, $SO_2NR_aR_b$, $CONR_aSO_2R_b$,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, or

; and

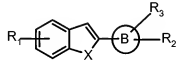
each R_a and R_b is independently selected from the group consisting of: hydrogen, (C_{1-6})alkyl, aryl, and (C_{1-6})alkyl-aryl;

where each said (C_{1-6})alkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, -N(R')$_2$, -CH_2N(R')$_2$, nitro, cyano, -CO_2R', -CON(R')$_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, -N(R')$_2$, -CH_2N(R')$_2$, nitro, cyano, -CO_2R', -CON(R')$_2$, -COR', and -NR'C(O)R'; ~~and~~

or a pharmaceutically acceptable salt thereof.

2. (Currently amended): A method of relaxing bladder smooth muscle tissue through the activation of large conductance calcium activated potassium channels, which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I):



(I)

wherein:

R_1 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, trifluoromethyl, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of:

halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

each R' is independently H or unsubstituted (C_{1-6})alkyl;

X is NR_a;

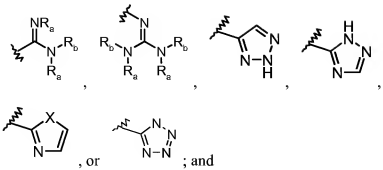
B is phenyl;

R_2 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

R_3 is COOH, $CONR_aR_b$, SO_3H, $SO_2NR_aR_b$, $CONR_aSO_2R_b$,



each R_a and R_b is independently selected from the group consisting of: hydrogen, (C_{1-6})alkyl, aryl, and (C_{1-6})alkyl-aryl;

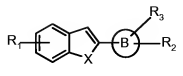
where each said (C_{1-6})alkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

or a pharmaceutically acceptable salt thereof.

3. (Cancelled)

4. (Currently amended): A pharmaceutical composition which comprises a compound according to formula (I):



(I)

wherein:

R_1 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, trifluoromethyl, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

each R' is independently H or unsubstituted (C_{1-6})alkyl;

X is NR_a;

B is phenyl;

R_2 is absent or represents up to three substituents independently selected from the group consisting of: (C_{1-6})alkyl, (C_{2-6})alkenyl, (C_{3-6})cycloalkyl, aryl, (C_{1-6})alkyl-aryl, OR_a, SR_a, hydroxy, halogen, nitro, cyano, COR_a, CO_2R_a, SO_3H, (C_{1-6})alkyl-CO_2-(C_{1-6})alkyl, $CONR_aR_b$, and NR_aR_b;

where each said (C_{1-6})alkyl, (C_{2-6})alkenyl, and (C_{3-6})cycloalkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

R_3 is COOH, $CONR_aR_b$, SO_3H, $SO_2NR_aR_b$, $CONR_aSO_2R_b$,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each R_a and R_b is independently selected from the group consisting of: hydrogen, (C_{1-6})alkyl, aryl, and (C_{1-6})alkyl-aryl;

where each said (C_{1-6})alkyl group is unsubstituted or substituted with 1 to 5 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

where each said aryl group is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of: halo, -OR', -SR', (C_{1-6})alkylsulfonyl, (C_{1-6})alkylsulfoxyl, $-N(R')_2$, $-CH_2N(R')_2$, nitro, cyano, $-CO_2R'$, $-CON(R')_2$, -COR', and -NR'C(O)R';

or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

5-15. (Cancelled)

16. (New) The method according to claim 1 wherein the disorder is urinary incontinence.

17. (New) The method according to claim 16 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein X is NR_a where R_a is hydrogen, (C_{1-6})alkyl, or (C_{1-6})alkyl-aryl, or a pharmaceutically acceptable salt thereof.

18. (New) The method according to claim 16 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein R_3 is COOH, or a pharmaceutically acceptable salt thereof.

19. (New) The method according to claim 16 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) which is:

3-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid;
3-(5,6-Dimethyl-1H-indol-2-yl)-benzoic acid;
3-(5,6-Dichloro-1H-indol-2-yl)-4-methoxy-benzoic acid;
5-(5,6-Dichloro-1H-indol-2-yl)-2-chloro-benzoic acid;
3-(5,6-Dichloro-1-methyl-indol-2-yl)-benzoic acid;
5-(5,6-Dimethyl-1H-indol-2-yl)-2-chloro-benzoic acid;
3-(5,6-Dimethyl-1H-indol-2-yl)-4-methoxy-benzoic acid;
5,6-Dichloro-2-[4-(1*H*-tetrazol-5-yl)-phenyl]-1*H*-indole;
3-(1-Benzyl-5,6-dichloro-1H-indol-2-yl)-benzoic acid; or
4-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid; or a pharmaceutically acceptable salt thereof.

20. (New) The method according to claim 1 wherein the disorder is an overactive bladder.

21. (New) The method according to claim 20 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein X is NR_a where R_a is hydrogen, (C_{1-6})alkyl, or (C_{1-6})alkyl-aryl, or a pharmaceutically acceptable salt thereof.

22. (New) The method according to claim 20 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein R_3 is COOH, or a pharmaceutically acceptable salt thereof.

23. (New) The method according to claim 20 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) which is:

3-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dichloro-1H-indol-2-yl)-4-methoxy-benzoic acid;

5-(5,6-Dichloro-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dichloro-1-methyl-indol-2-yl)-benzoic acid;

5-(5,6-Dimethyl-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-4-methoxy-benzoic acid;

5,6-Dichloro-2-[4-(1*H*-tetrazol-5-yl)-phenyl]-1*H*-indole;

3-(1-Benzyl-5,6-dichloro-1H-indol-2-yl)-benzoic acid; or

4-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid; or a pharmaceutically acceptable salt thereof.

24. (New) The method according to claim 1 wherein the disorder is pollakiuria.

25. (New) The method according to claim 24 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein X is NR_a where R_a is hydrogen, (C_{1-6})alkyl, or (C_{1-6})alkyl-aryl, or a pharmaceutically acceptable salt thereof.

26. (New) The method according to claim 24 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein R_3 is COOH, or a pharmaceutically acceptable salt thereof.

27. (New) The method according to claim 24 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) which is:

3-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dichloro-1H-indol-2-yl)-4-methoxy-benzoic acid;

5-(5,6-Dichloro-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dichloro-1-methyl-indol-2-yl)-benzoic acid;

5-(5,6-Dimethyl-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-4-methoxy-benzoic acid;

5,6-Dichloro-2-[4-(1*H*-tetrazol-5-yl)-phenyl]-1*H*-indole;

3-(1-Benzyl-5,6-dichloro-1H-indol-2-yl)-benzoic acid; or

4-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid; or a pharmaceutically acceptable salt thereof.

28. (New) The method according to claim 2 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein X is NR_a where R_a is hydrogen, (C_{1-6})alkyl, or (C_{1-6})alkyl-aryl, or a pharmaceutically acceptable salt thereof.

29. (New) The method according to claim 2 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) wherein R_3 is COOH, or a pharmaceutically acceptable salt thereof.

30. (New) The method according to claim 2 which comprises administering to a subject in need thereof an effective amount of a compound according to formula (I) which is:

3-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dichloro-1H-indol-2-yl)-4-methoxy-benzoic acid;

5-(5,6-Dichloro-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dichloro-1-methyl-indol-2-yl)-benzoic acid;

5-(5,6-Dimethyl-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-4-methoxy-benzoic acid;

5,6-Dichloro-2-[4-(1*H*-tetrazol-5-yl)-phenyl]-1*H*-indole;

3-(1-Benzyl-5,6-dichloro-1H-indol-2-yl)-benzoic acid; or

4-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid; or a pharmaceutically acceptable salt thereof.

31. (New) The pharmaceutical composition according to claim 4 which comprises a compound according to formula (I) wherein X is NR_a where R_a is hydrogen, (C_{1-6})alkyl, or (C_{1-6})alkyl-aryl, or a pharmaceutically acceptable salt thereof.

32. (New) The pharmaceutical composition according to claim 4 which comprises a compound according to formula (I) wherein R_3 is COOH, or a pharmaceutically acceptable salt thereof.

33. (New) The pharmaceutical composition according to claim 4 which comprises a compound according to formula (I) which is:

3-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-benzoic acid;

3-(5,6-Dichloro-1H-indol-2-yl)-4-methoxy-benzoic acid;

5-(5,6-Dichloro-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dichloro-1-methyl-indol-2-yl)-benzoic acid;

5-(5,6-Dimethyl-1H-indol-2-yl)-2-chloro-benzoic acid;

3-(5,6-Dimethyl-1H-indol-2-yl)-4-methoxy-benzoic acid;

5,6-Dichloro-2-[4-(1*H*-tetrazol-5-yl)-phenyl]-1*H*-indole;

3-(1-Benzyl-5,6-dichloro-1H-indol-2-yl)-benzoic acid; or

4-(5,6-Dichloro-1H-indol-2-yl)-benzoic acid; or a pharmaceutically acceptable salt thereof.